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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,410	01/18/2005	Axel Ullrich	2923-679	7025

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EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
11/17/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/521,410	**Applicant(s)** ULLRICH ET AL.	
	Examiner Peter J. Reddig	**Art Unit** 1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 October 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *10,12,14,17-19 and 35*.
   Claim(s) withdrawn from consideration: *1-9, 11, 13, 20-34*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Karen A Canella/
Primary Examiner, Art Unit 1643

Continuation of 5. Applicant's reply has overcome the following rejection(s): The rejection of claims 10, 12, 14, 17-19, and 35 under 35 U.S.C. 112, second paragraph in section 5, pages 5-6, the rejection of claims 10, 12, 14, 17-19, and 35 under 35 U.S.C. 112, first paragraph in section 6, pages 6-7, and claims 10, 12, and 14 under 35 U.S.C. 102(b), in section 7 pages 7-8 of the Final Rejection of May 14, 2008.

Continuation of 11. does NOT place the application in condition for allowance because: Claims 10,12,14,17-19 and 35 remain rejected for the reasons set under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement essentially for the reasons set forth in the Office Action of May 14, 2008, sections 4, pages 2-5.

Applicants argue that the Examiner alleges that one of skill in the art would not predictably be able to reduce the invasivity of cancer cells that are susceptible to AXL suppression in vivo. Applicants disagree with the Examiner's allegation and submit herewith references, Voskoglou- Nomikos et al. (Clinical Research, vol. 9, 4227-4239, 2003) and Khleif et al. (Animal Models in Developmental Therapeutics, Chapter 42, p. 573-584, 2000), in support of the enablement of those skilled in the art to use the presently claimed methods at the time the invention. Voskoglou-Nomikos et al. assess the clinical predictive value of the in vitro cell line, human xenograft, and mouse allograft pre-clinical models. The results suggest that the in vitro cell line model is of at least equivalent usefulness to the human xenograft model (see page 4237, left column, second paragraph). Further, the author argue for "emphasis to be placed on in vitro cell lines (in the context of the NCI HumanTumor Cell Line Screen) and appropriate panels of the human xenograft model."

Applicants' arguments have been considered, but have not been found persuasive becauseVoskoglou-Nomikos et al. filed after final has not and will not be entered because Applicants have failed to provide good and sufficient reasons why it was not submitted eariler and thus the evidence therein has not been considered. Thus arguments based on the evidence in Voskoglou-Nomikos et al. are moot and claims 10,12,14,17-19 and 35 remain rejected for the reasons previously set forth.

Khleif et al. discuss the role of animal models in drug discovery and drug screening. The reference describes that National Cancer Institute's (NCI) current cancer screening method as "an in vitro (Stage I) screen followed by the more refined in vivo (Stage II) screen" (see paragraph bridging pages 573-574). In particular, it can be seen from this reference that the implantation of tumor cells is a generally accepted model for drug development. Further, the authors describe several approaches for tumor implantation (pages 577-578). Applicants argue that on page 576, right column, 3rd full paragraph, that Khleif et al. refer to the success of human tumor xenografting into nude mice as "revolutionizing many aspects of cancer research, including drug development." The reference further states "in fact, excellent correlations can be made between average growth delay for human tumors in nude mice treated with the best available drug combinations and complete clinical response rates"; studies using lung cancer, colon cancer, breast cancer, and malignant melanoma are cited (see page 577, 1st full paragraph). Moreover, Khleif et al. discuss the refinement of animal models in drug development over time, mentioning the "general convertability of doses between species" (see page 581, right column, last paragraph). Based on the above reasoning, Applicants argue tha claim 10 is allowable and claims 12, and 14-19, depending from claim 10, are allowable for at least the above reasons.

Applicants' arguments have been considered, but have not been found persuasive because Khleif et al. filed after final has not and will not be entered because Applicants have failed to provide good and sufficient reasons why it was not submitted eariler and thus the evidence therein has not been considered. Thus arguments based on the evidence in Khleif et al. are moot and claims 10,12,14,17-19 and 35 remains rejected for the reasons previously set forth.